CHAPTER III: MIND-BODY MEDICINE

Cancer

What I want to do now is turn to how, in medicine, we can use some of these lessons in a different approach that involves providing emotional support to cancer patients, which has been another major line of research. Here are some of my colleagues at Stanford, and elsewhere, who have worked with me over many years, in this line of research. Here again is that maquette that my patient did, showing her modified radical mastectomy, transflap reconstruction, and radiation burns. Cancer patients live with daily, constant reminders of the effects of the illness. Cheryl Koopman in my lab found that the rates of posttraumatic stress disorder symptoms, the kind you seen in Vietnam and Gulf War veterans, the kind you see in rape victims, are about as high in metastatic breast cancer patients. That's the pink stippled bars here. So many of them suffer with the same intrusive recollections, the lack of pleasure and usually pleasurable activities, and the irritability that you see in people with posttraumatic stress disorder. Cancer patients also suffer with depression. This was done by a Dutch breast cancer patient, and one of the most remarkable things about this is that it's the only work of art she did in her life, and I think it's just a remarkable work of art. In fact, the rate of major depression increases with the severity of medical illness. So a substantial minority of people with cancer and other serious illnesses suffer from the hopelessness, helplessness, and worthlessness that is typical of depression as well. So we have range from the minor kind of acute stress that I talked about at the beginning, to rather severe posttraumatic stress and major depressive symptoms in patients with cancer. This can not only affect the way they adjust to cancer, but it can actually increase risk for cancer. This paper was published in the *Journal of the National Cancer Institute* several years ago by Brenda Penninx. She found that if you had major depression on 3 separate episodes, so you have chronic and severe depression, you have an almost twofold elevated risk of getting cancer. The literature now is divided, but about 2:1, the studies indicate that major depression increases the risk of getting cancer or more rapid progression of cancer.

Now why might that be? What's going on that could link the sort of maladaptive stress response, depression, to some actually more rapid progression of tumor? I'm going to talk about particularly the hormonal system but also about the immune system to give you an idea of what we're learning. Bear in mind that one of the sort of daily cycles that our normal bodies have is alteration in a stress hormone called cortisol. I'll describe it in a minute, but the point of this slide is to show that your cortisol, waking up, as you know from this morning, is a daily stress test. Your cortisol is 4 times higher in the morning than it is in the evening when you go to sleep. You should be down here about now. But if you're depressed, your cortisol levels tend to remain high all the time. So you've lost this nice daily variation or cycling in cortisol. People with posttraumatic stress disorder tend to have flat and low cortisol patterns. But both are abnormal. Both do not have this nice, normal, daily variation. Cortisol is produced in the adrenal cortex. It helps the body produce glucose in the blood; sugar so that your muscles can fight or flee and your brain has plenty of sugar to think about what it is you're going to do. But it's a system that is designed to shut itself off as soon as the cortisol levels have gone up. There are a number of levels of control. Typically, it turns on when you're stressed and turns off as soon as the cortisol level starts to rise. However, when you're chronically stressed, the situation called allostatic load can occur. Bruce McEwen at Rockefeller described this as an accumulation of chronic stressors that tend to keep the system stuck in either the on or the off position as you see here. So it's like a light switch that's overused. You keep turning it on, and eventually, the light either just stays on all the time here or it doesn't go on at all. It's off all the time. This is a maladaptive stress response. Now we looked at the cortisol patterns in our metastatic breast cancer patients, and this was in a study that was funded by the National Institute of Mental Health (NIMH) and the National Cancer Institute (NCI). We found that only about 1/3 of them had normal patterns like this blue line. Others had abnormal patterns in which the cortisol levels would actually go up later in the day. So they were acting as though they were accumulating more and more stress, and their bodies were in this stress mode all the time. If you divided them into the relatively normal and the relatively abnormal cortisol patterns, we found that we could predict mortality up to 7 years later. The patients with the relatively abnormal patterns tended to die sooner than the patient's with the abnormal patterns. So the maladaptive

stress response, reflected in this abnormal daily pattern of the hormone cortisol, turns out to predict mortality years later. In fact, it was the women who had lost social support, who were widowed, divorced, or separated, who were more likely to have these abnormal patterns. It might interest you to know that the women who never made the mistake of getting married in the first place had quite normal patterns. But if you had the relationship and lost it, you seemed to show this stress pattern. Now there's accumulating evidence. This is a study done by a French group that took mice and ablated the part of the brain that actually regulates this diurnal pattern. It's called the suprachiasmatic nucleus. They then implanted tumors in those mice, and they found that the ones that had the disrupted cortisol patterns had tumor growth that was more than twice as rapid. So there seems to be something about this daily pattern of this stress hormone, cortisol, that is a regulator of the rate of tumor growth. When these patterns are abnormal, tumors tend to grow more rapidly.

One other mechanism by which this may work involves the immune system. Our patients who had these abnormal cortisol patterns had lower numbers of what are called natural killer cells. They're lymphocytes that attack transformed or dying cells that are involved in cancer surveillance. Cortisol other glucocorticoids are potently immunosuppressive. That's why we take corticosteroids when we have autoimmune disease like arthritis. So there's something going on in the body here in which these persistent levels of cortisol seem to be immunosuppressive, and this may be one way in which the abnormal cortisol pattern has an effect on the rate of cancer progression. We also found that patients high in cortisol had lower delayed type hypersensitivity. When we injected antigens under the skin like a TB test, we found that those with the high cortisol levels were more likely not to respond to these antigenic stimuli that were stuck under the skin. So these patients seemed relatively immunosuppressed as well.

If there's some relationship between this abnormal stress pattern, what does that have to do with the mind? We talked about the body and cancer. How can we do something about the mind that might have an effect on the rate of cancer progression? One of the

hopes of mind-body medicine is that we can help people live better and perhaps even live longer.

We have evidence that this same pattern of disrupted cortisol rhythm is associated with a maladaptive way of handling the kind of emotional distress that I talked about at the beginning of the lecture. People who repress all feelings, who don't let themselves feel anything—those in particular who can't allow themselves to experience some negative emotion for some period of time—are more likely to have this pattern. I'll show you quickly how we measure that. This is a line that represents the rate of change in cortisol over time. The steeper lines here are the more normal ones. You see that the very anxious or the very repressed people have relatively abnormal cortisol patterns. These are, again, statistically significant differences. If people don't handle their emotions well, it's as if they put off the acute crisis but pay a price by being chronically in this stressed mode. We code emotion looking at videotapes of these patients in support groups. She's saying, "Cheer up," and the boy is saying, "Cheer down." Some people just don't handle emotional reassurance very well. The boy is one of them. A team of raters will look at videotape and actually score how long these patients can tolerate expressing emotion. We computer code that. We have found that patients who are better at allowing themselves to experience negative feelings such as fear, sadness, and anger have more normal cortisol patterns than the one who can't. This, by the way, goes very much against the pop idea that if you let yourself be upset about cancer you're giving in to the cancer. My patients call that the prison of positive thinking. One of my patient's husbands said, "Don't cry, you'll make the cancer spread." Nothing could be farther from the truth—it's a good thing he wasn't in the room at the time, he would have been in big trouble. But there are a lot of pop authors who tell you that. They say that if you let yourself give in to fear or sadness about cancer, you're giving in to the disease. We think, if anything, that the opposite is the case. If you can allow yourself to experience genuine emotions that come with the cancer, your body may do better, not worse. As usual, Shakespeare said it best. He said:

Give sorrow words;
the grief that does not speak,

Whispers the o'er-fraught heart
and bids it break.

What I want to do now is show you how we work with these findings to try and help people cope better with cancer in group therapy. This is one model, if you're psychoanalytically inclined, but we actually use chairs, not couches. Our model of providing support involves building a new network of social support and encouraging people to give vent to their emotions as they come. Build new bonds of support, express emotion, detoxify fears of dying and death, reorder priorities in life, improve family relationships, clarify communications with doctors, and the kind of self-hypnosis that I talked earlier about.

I want to focus on a couple of them, particularly expressing emotion. We think that facing feelings directly can be a source of closeness. It can help people modulate their reaction to these feelings, and as I showed you with that picture early on looking at 9-11, one powerful way to modulate emotion is to have 2 emotions going on simultaneously. My patients find that it is very different to wake up at 2 o'clock in the morning wondering if you'll live to see your daughter get married, than it is to talk about it with 8 other people who have the same problems at 2 o'clock in the afternoon on Wednesday. It's the same fear, the same problem, but you experience it very differently when you're surrounded by people who are going through the same situation. Thomas Jefferson said, "When angry, count 10 before you speak. If very angry, count 100." Mark Twain said, "When angry, count 4, when very angry, swear." We're more on the Mark Twain side of this equation.

Now one of the things that will arouse strong emotion is people's existential concerns—t heir fears of dying and death. We were very worried when we started this that we might demoralize people, but in fact, we find that patients can be the stronger for facing what they most fear, even the death of other people in the group. I want to show you now a segment of videotape in which members of our group were just reacting to news that the first member of the group had died.

"What happened?"

"I'd like to know what happened."

"My understanding is that she got some fluid in her lungs and that a decision was made not to be extremely aggressive in trying to treat that, that they felt the prognosis wasn't good."

"I'm angry that I didn't have a chance to say goodbye. I mean, it just feels so abrupt."

"Cheated."

"And we weren't able to do anything not knowing."

"You would have wanted to be able to. . ."

"Well, at least I would have sent. . ."

". . .flowers."

"Yeah, something."

"The issue that I hear everyone talking about is the lack of predictability. A sense that here was Debbie, talking about her trip to Hawaii, and now she's not with us."

"There was a big bubble there of euphoria for her, and it was gone, and it wasn't a bubble, it was a big, deep hole."

"I wish I had known her better. I wish I had known her before cancer. I keep thinking, "What was she like before?" We never really knew the real Debbie because she said that that wasn't the real Debbie."

"I invested in her. I had feelings for her."

"Can you tell us about your feelings?"

"I just wish I could talk to her."

"I would have liked to say goodbye."

"Something."

"What would you say to her?"

"Not to worry. Not to fear. And to have somebody there to tell you that. And just share with her that it's okay. That her family will be okay. They will be all right. And for her not to feel guilty for being sick and guilty for dying on them. And they will continue."

What you're doing in that group is marching death right there in the center of that circle and forcing those women to look at it. They can't turn their eyes away from it. You're rubbing their nose in it. Can that be good for you?

Maurice has such a gentle way of asking questions. He told me that journalists are people who explain things they don't understand, which I like. But he's right, we are rubbing their nose in it. Yet I think that as you watch these women deal with this bad news, they were doing some interesting things. First of all, they came up with things I never would have thought of —to not feel guilty for dying on them. You know what? Dying people do feel guilty. They feel that they're letting their loved ones down, even though they have no control over it. Furthermore, what they're doing is figuring out a better way to die.

They're saying that part of what's bad is that she died; part of what's bad is that she died so suddenly that we couldn't say goodbye to her. There were things we wanted to say. So they're sort of creating norms for a better way to die. That's a way of gaining control over the process of dying, even while they're facing the ultimate helplessness, which is that we all die, and we'll be taken from our loved ones. So they're dealing with it. It's sad; they're upset, but they're learning to cope with it. Many patients report that they feel better for being able to do it. When one of our patients died, another who was a poet made these little cards that she handed out:

"Dear Eva, Whenever the wind is from the sea, salty and strong, you are here. Remembering your zest for hilltops and the sturdy surf of your laughter gentles my grief at your going and tempers the thought of my own."

Another woman said that "being in the group is like the fear you have standing at the top of a tall building or the edge of the Grand Canyon. At first you're afraid to even look down; I don't like heights, but gradually you learn to do it, and you can see that falling down would be a disaster, nonetheless, you feel better about yourself because you're able to look. That's how I feel about death in the group. I can't say I feel serene, but I can look at it."

So when you take these stressors, face them head-on, deal with the emotions that come, people emerge from that feeling prepared, feeling stronger. One patient said, "I watched a friend of mine die last week. It wasn't pretty, but it wasn't that terrible. I realized for the first time that I could do it." We isolate ourselves from death and dying so much in this culture that many people have never seen a person die. They don't know what it's like. They don't know how to do it. One of my patients said, "Why is it that we're so into natural childbirth and artificial death?" Death is a natural part of life. It's a very precious and important time in life if it's done properly, and this is one way to help prepare people for it.

I had occasion to present this work to the Dalai Lama when he visited Stanford. He's a wonderful, intelligent, smart, playful, serious man all at once. I asked him—because many docs were worried we'd make patients worse when we did this, that we'd demoralize them— from his Buddhist perspective why he thought it could be helpful. He thought for a minute, and he said, "I have a very busy travel schedule," and I thought, "We're not communicating here." Then he said, "And it makes me anxious. And when I get anxious about it, I call over one of my assistants, and I ask him what am I doing for the next few days, and he tells me, and I feel better." He said, "That's the way we Buddhists feel about death. We make it familiar, and it becomes less frightening." So he got it exactly right. That's exactly what's going on. I think our avoidance of death ultimately makes it even more frightening than it already is.

Facing your death also helps people reorder their priorities in life, face the things they need to face, do what's important, and trivialize the trivial in their life. My colleague and mentor, Herb Rollins says, "Cancer cures neurosis." You just don't have time for it because there are more important things, although not everybody gets it.

"I'm sorry Mr Rainey, our tests show you have 2 weeks to live," and he says, "Can I take them in August?" For those who are interested, we have a book published by Basic Books that goes in more detail into the techniques involved in supportive, expressive group therapy with Catherine Clausen**.**

Well, does it work? We did a randomized trial here. We found that over the course of a year, women who were in our supportive/expressive group therapy had a significantly greater reduction in traumatic stress symptoms on a measure called the impact of events scale than the control patients. So yes, despite the fact that they are watching one another die, they're dealing with these issues of dying and death, they're expressing painful emotions. They are less anxious. They're less irritable. They're less preoccupied with the illness than those in the routine care control condition, so it helps psychologically. We also found that we reduced their tendency to suppress emotion. So they're more open to their own feelings, and we think, therefore, can deal with them better than control

patients who get routine care. They also feel more in control of how they deal with their emotions. Many people are afraid that letting go of their sadness or anger will be like opening Pandora's box; it'll never stop. In fact, these women feel more competent. They feel like experts in living and experts in dealing with the emotions that come with the stress of serious illness. They're less repressed and less defensive as well. So from a number of measures, we're able to help these patients manage their emotions better and reduce their distress. The interesting thing is that the effect in reducing traumatic stress symptoms is mediated by the change in emotional control. So by giving vent to these emotions in the group, you're actually reducing their overall distress.